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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,447	07/09/2007	Tomoaki Takakura	0032-0291PUS1	4157

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER

EPPS -SMITH, JANET L

ART UNIT	PAPER NUMBER
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1633

NOTIFICATION DATE	DELIVERY MODE
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02/02/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/584,447	Applicant(s) TAKAKURA ET AL.	
	Examiner Janet L. Epps-Smith	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 July 2007 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06/28/2007;02/11/2008</u> . | 6) <input checked="" type="checkbox"/> Other: <u>notice to comply</u> . |

DETAILED ACTION

1. Claims 1-16 are presently pending for examination.

Drawings

2. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the details of Figure 1 cannot be discerned. For example, the numbers on the graphs are so small that they cannot be read. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Sequence Information

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification as filed makes mention of SEQ ID NO: 1-3, however there is no Sequence Listing of record.
4. A complete response to this Office Action requires that Applicants comply with the sequence rules, and that pending rejections be addressed. Any response that does not address all of these issues will be held as non-responsive. Direct the reply to the

Art Unit: 1633

undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 (and those claims dependent thereon, claims 2-15) recite: “[A] process for producing a protein-polymer complex, comprising a step of reacting a protein conjugated with a polymer thereto with a compound having a mercapto group to eliminate a polymer which is ester-bound to a mercapto group of a cysteine residue of the protein.” The metes and bounds of this process are vague and indefinite since it is unclear if the polymer mentioned in the third line of the process is intended to be the same or distinct as the polymer mentioned in the fourth line.

8. Furthermore, the process set forth in claims 1-15 appears to be incomplete since the objective of the process is “for producing a protein-polymer complex,” however the actual method steps result in the elimination of the polymer group from the protein-polymer complex.

9. Claim 16 recites “[A] method for eliminating a polymer which has ester-bound to a mercapto group of a cysteine residue of the protein, comprising reacting a protein conjugated with a polymer thereto with a compound having a mercapto group.” The

Art Unit: 1633

metes and bounds of this method are vague and indefinite since it is unclear if the polymer recited in the first line of the claim is the same polymer recited in the third line of the claim. Line 2 of this claim recites the term "the protein," there is lack of antecedent basis for this limitation in the claim. Also, it is unclear if the term "a protein," recited in line 3 of this claim corresponds to the same protein recited in line 2 of this claim. Thus the scope of the claimed method is unclear.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 11, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Tan et al. (WO96/40284A1).

12. Claim 11 recites a protein-polymer complex obtained by a process as defined in any one of claims 1 to 10. Claim 13 recites a methioninase-polyethylene glycol complex or transglutaminase-polyethylene glycol complex obtained by a process as defined in claim 12. As per MPEP § 2113[R-1] "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964,

Art Unit: 1633

966 (Fed. Cir. 1985) (citations omitted). Thus the disclosure of Tan et al. at page 86 as described below which discloses the methioninase-polyethylene glycol complexes read on the claimed invention.

Claim 14 is drawn to a methioninase-polymer complex, which has average 3.1 or more of free mercapto groups per 1 subunit. Claim 15 is drawn to an anti-tumor agent, containing a methioninase-polymer complex as defined in claim 13 or 14. According to the specification as filed at paragraph [0041]: “[F]or example, when a protein is methioninase, the protein is a tetramer consisting of four subunits, and each subunit has ten amino groups (including an N-terminal amino group) and four mercapto groups.” Therefore, absent evidence to the contrary the disclosure of Tan et al. at page 86 reads on the claimed invention. Tan et al. discloses the following: (1) A chemically modified methioninase comprising methioninase conjugated to a polymer, wherein the polymer is polyethylene glycol. Furthermore, Tan et al. discloses a method of treating a patient having a tumor comprising the step of administering to said patient a therapeutically effective amount of the methioninase-polymer composition.

13. Claims 11, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Tan et al. (1998; Protein Expression and Purification, Vol. 12, pages 45-52.)

14. Tan et al. disclosed PEGylated Methioninase as a treatment for cancer. See page 48, last paragraph:

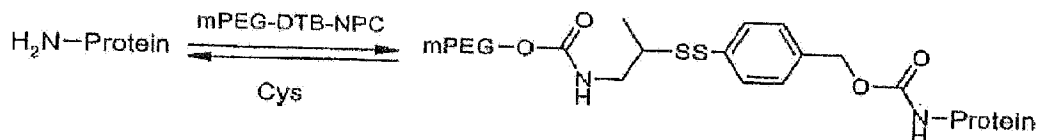
Art Unit: 1633

Growth Inhibitory Effect of PEG-rMETase on Human Cancer Cells in Vitro

Human normal and tumor cells were incubated in methionine-containing RPMI 1640 medium supplemented with 10% fetal bovine serum with PEG-rMETase or rMETase (0.005–4 units/ml) for 72 h at 37°C/5% CO₂. After the 72-h incubation period, the cells were counted with a hemocytometer and relative growth rates were calculated.

15. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Zalipsky et al. Due to the ambiguity associated with this claim, for the reasons set forth above. The prior art is applied to the extent that it discloses a method comprising reacting a protein conjugated with a polymer thereto with a compound having a mercapto group.

16. Zalipsky et al. describe the following reaction which involves the reaction of cysteine with a protein-polymer conjugate to eliminate the ester bound polymer:



Art Unit: 1633

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/
Primary Examiner, Art Unit 1633